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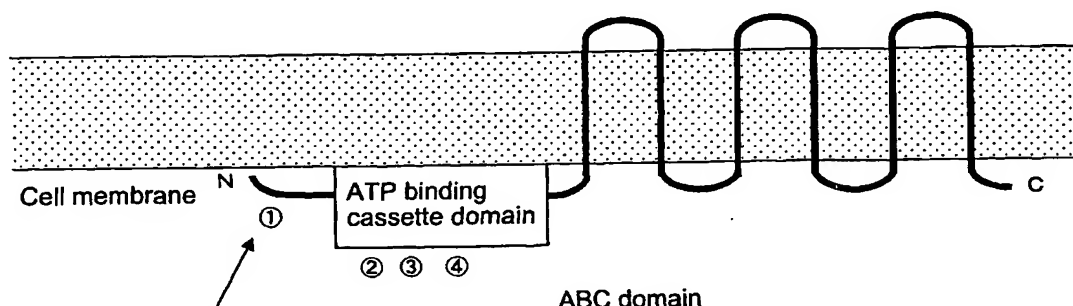
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[Continued on next page]

(54) Title: METHOD FOR PREDICTING A DRUG TRANSPORT CAPABILITY BY ABCG2 POLYMORPHISMS



Leader sequence

① 34G→A (Val12Met)

ABC domain

② 376C→T (Gln126Term)

③ 421C→A (Gln141Lys)

④ 458C→T (Thr153Met)

(57) Abstract: The present invention provides polymorphisms of ABCG2 polypeptide and polynucleotide coding therefor, which is related to the intracellular accumulation of indolocarbazole compounds, as well as methods for detecting the polymorphisms, comprising collecting a sample from mammals, and determining a polymorphism of the nucleotide sequence of ABCG2 gene or a polymorphism of the amino acid sequence of ABCG2 polypeptide. In a preferred embodiment of the present invention, the polymorphism of the nucleotide sequence is one or more of single nucleotide polymorphisms at positions selected from the group consisting of 34, 376 and 421 of SEQ ID NO:1, and the polymorphism of the amino acid sequence is one or more of amino acid polymorphisms at positions consisting of 12, 126, and 141 of SEQ ID NO:2.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G06F19/00 C12Q1/68 C07K14/47 C07K16/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, EMBL, WPI Data, PAJ, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>NAKATOMI KATSUMI ET AL: "Mutation and quantitative analysis of breast cancer resistance protein (BCRP/MXR/ABCG2) gene in lung cancer cells and tumor tissues" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, vol. 43, March 2002 (2002-03), page 778 XP001155530</p> <p>93rd Annual Meeting of the American Association for Cancer Research; San Francisco, California, USA; April 06-10, 2002, March, 2002</p> <p>ISSN: 0197-016X</p> <p>the whole document</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1,5,7, 16,17

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

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Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>HONJO YASUMASA ET AL: "Single-nucleotide polymorphism (SNP) analysis in the ABC half-transporter MXR/BCRP/ABCP1/ABCG2" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, vol. 43, March 2002 (2002-03), pages 778-779, XP001155529 93rd Annual Meeting of the American Association for Cancer Research; San Francisco, California, USA; April 06-10, 2002, March, 2002 ISSN: 0197-016X the whole document</p>	9-11, 14-18
X	<p>ALLEN JOHN D ET AL: "A mutation hot spot in the Bcrp1 (Abcg2) multidrug transporter in mouse cell lines selected for doxorubicin resistance" CANCER RESEARCH, vol. 62, no. 8, 15 April 2002 (2002-04-15), pages 2294-2299, XP002256815 ISSN: 0008-5472 abstract page 2295, left-hand column, paragraph 2 page 2296, left-hand column, paragraph 2 -page 2298, left-hand column, paragraph 1 figure 3</p>	1,12,14, 15,22
X	<p>DOYLE L A ET AL: "A MULTIDRUG RESISTANCE TRANSPORTER FROM HUMAN MCF-7 BREAST CANCER CELLS" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, December 1998 (1998-12), pages 15665-15670, XP001055044 ISSN: 0027-8424 cited in the application page 15665, right-hand column, paragraph 3</p>	12,14, 15,22
X	<p>WO 02 28894 A (BANYU PHARMA CO LTD ; HARA YOSHIKAZU (JP); KOMATANI HIDEYA (JP); KO) 11 April 2002 (2002-04-11) cited in the application the whole document</p>	1,12,14, 15,22
X	<p>DATABASE EMBL 'Online! EBI; 21 October 2001 (2001-10-21) NCI-MGC: "603176769F1 NIH_MGC_121 Homo sapiens cDNA clone IMAG:5240944 5'" retrieved from HTTP://WWW.EBI.AC.UK Database accession no. BI918550 XP002256817 the whole document</p>	9-12,14, 15,22

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>HONJO Y ET AL: "Acquired mutations in the MXR/BCRP/ABCP gene alter substrate specificity in MXR/BCRP/ABCP-overexpressing cells" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 61, no. 18, 15 September 2001 (2001-09-15), pages 6635-6639, XP002228052 ISSN: 0008-5472 abstract page 6636, right-hand column, paragraph 1 -page 6639, left-hand column, paragraph 3 table 1 figure 1</p>	1
P,X	<p>-----</p> <p>IMAI YASUO ET AL: "C421A polymorphism in the human breast cancer resistance protein gene is associated with low expression of Q141K protein and low-level drug resistance" MOLECULAR CANCER THERAPEUTICS, vol. 1, no. 8, 17 June 2002 (2002-06-17), pages 611-616, XP002256816 ISSN: 1535-7163 abstract page 612, left-hand column, paragraph 3 -page 616, left-hand column, paragraph 3 tables 1-3 figure 5</p>	1-7, 9-20,22, 23
P,X	<p>-----</p> <p>IIDA A ET AL: "Catalog of 605 single-nucleotide polymorphisms (SNPs) among 13 genes encoding human ATP-binding cassette transporters: ABCA4, ABCA7, ABCA8, ABCD1, ABCD3, ABCD4, ABCE1, ABCF1, ABCG1, ABCG2, ABCG4, ABCG5 and ABCG8" JAPANESE JOURNAL OF HUMAN GENETICS, TOKYO, JP, vol. 47, no. 6, 28 June 2002 (2002-06-28), pages 285-310, XP002966806 ISSN: 0916-8478 page 304 page 308, left-hand column, paragraph 5 -right-hand column, paragraph 1</p>	9-18,22
E	<p>-----</p> <p>EP 1 323 735 A (BANYU PHARMA CO LTD) 2 July 2003 (2003-07-02) examples 4-6,10-14</p>	1,12,14, 15,22

INTERNATIONAL SEARCH REPORT

International application No.
T/JP 03/07534

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 23
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(v) PCT - Presentation of information
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
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